BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 48(10), 2993—2994 (1975)

Synthesis and NMR Spectra of *para*-Substituted Benzyl Hydrodisulfides and Related Compounds

Shunichi KAWAMURA, Toyokazu HORII, Takeshige NAKABAYASHI, and Masayuki HAMADA
Radiation Center of Osaka Prefecture, Shinke-cho, Sakai, Osaka 593

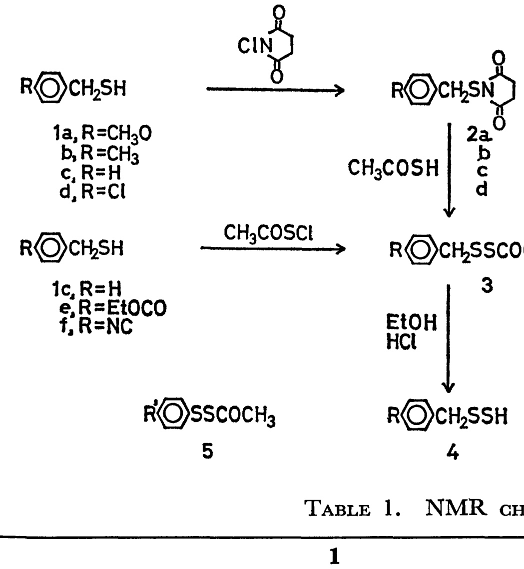
(Received May 29, 1975)

Synopsis. The titled compounds were synthesized and their NMR spectra were measured. The chemical shifts of benzyl hydrodisulfides were not related to σ or σ_R, while those of the corresponding thiols were related to σ.

In an NMR study of *para*-substituted phenyl hydrodisulfides, we have found a novel correlation for the chemical shifts of the mercapto protons.[1] The correlation, $\tau_{SSH}=0.263\sigma_R+6.653$ ($r=0.993$),[2] includes the chemical shift which is only related to the resonance term, and includes also a large positive ρ value. It has thus been postulated that the substituent effect in the *para*-substituted phenyl hydrodisulfides is conducted to the terminal protons anisotropically.

In the present work, the synthesis of *para*-substituted benzyl hydrodisulfides through a slightly modified route has been attempted, and the NMR spectra of the compounds have also been measured. The chemical shifts of mercapto and methylene protons of the compounds are interesting, because different correlations for the two kinds of protons are anticipated; the chemical shifts of mercapto protons should be related to σ_R, and those of methylene, to σ.

α-Toluenethiols having methoxy, methyl, or chlorine at the *para*-position (**1a**, **1b**, and **1d**) were allowed to react with *N*-chlorosuccinimide, giving *N*-(*p*-substituted benzylthio)succinimides in 22—35% yields (**2a**, **2b**, and **2d**).[3] By the condensation of the *N*-aralkylthiosuccinimides with thioacetic acid, acetyl *p*-substituted benzyl disulfides (**3a**, **3b**, and **3d**) were obtained in moderate yields. This reaction is an application of the synthesis of thiolsulfonates from *N*-(arylthio)-succinimides and arenesulfinic acids.[4] Acetyl disulfides **3e** and **3f** were prepared by the reactions of **1e** and **1f** with acetylsulfenyl chloride, respectively.[5] Compound **3c** could be obtained by both methods mentioned above. The acetyl *p*-substituted benzyl disulfides obtained were ethanolyzed in the presence of hydrogen chloride. Of the resulting hydrodisulfides, **4b**, **4d**, and **4e** were distilled under high vacuum to give products in 18—54% yields. However, **4a** and **4f** were unstable on distillation; in the case of **4a**, only 2.5% of the product was isolated and no product was obtained for **4f** (see experimental). The hydrodisulfides **4a**—**f** were stable in solvents such as carbon tetrachloride and chloroform.



The chemical shifts of the benzyl hydrodisulfides and related compounds are shown in Table 1. The chemical shifts of mercapto protons of *p*-substituted α-toluenethiols fit the thermodynamic relationship, $\tau_{SH}=-0.149\,\sigma+8.496$ ($r=0.978$). The ρ value (-0.149) is about a half of that for benzenethiols,[6] which is reasonable because it has been demonstrated that the insertion of methylene carbon atom into a side chain (in the present case, $R-C_6H_4-CH_2-SH$) diminishes ρ to 1/2—1/3 of its original value.[7] For the methylene protons of the α-toluenethiols, $\tau_{CH_2}=-0.103\sigma+6.330$ ($r=0.929$) was obtained. The correlation coefficient is not sufficiently large, and ρ is too small for protons of $R-C_6H_4-CH(SH)-\mathbf{H}$. These facts imply that some other effects, *e.g.*, a stereochemical effect as well as an electronic effect, reflect the chemical shift of the protons.

The chemical shifts of protons (both SSH and CH_2) of *p*-substituted benzyl hydrodisulfides **4** were related

TABLE 1. NMR CHEMICAL SHIFT DATA (in CCl_4, τ, ppm)

R	1		4		3[a]		5[b]
	$-CH_2-$	$-SH$	$-CH_2-$	$-SSH$	$-CH_2-$	$-CH_3$	$-CH_3$
MeO	6.359	8.532	6.199	7.300	6.102	7.646	7.628
Me	6.352	8.528	6.196	7.303	6.096	7.655	7.603
H	6.309	8.4875	6.156	7.289	6.066	7.662	7.578
Cl	6.332	8.463	6.193	7.277	6.114	7.635	
EtOCO	6.268	8.437	6.128	7.2815	6.0445	7.648	
NC	6.262	8.382	6.142	7.250	6.063	7.628	

a) In $CDCl_3$. b) Some other acetyl phenyl disulfides were measured: for EtO, 7.628; *t*-Bu, 7.592; Me_3Si, 7.576; F, 7.600; Br, 7.587.

Table 2. Acetyl *p*-substituted benzyl disulfides, $RC_6H_4CH_2SSCOCH_3$

	R	Mp, °C	Yield, %	Found (Calcd) %			
				C	H	N	S+Cl
3a	CH_3O	22	77	52.60 (52.55)	5.30 (5.37)		28.08 (27.96)
3b	CH_3	36.5—37.5	55	56.57 (56.60)	5.70 (5.77)		30.20 (29.66)
3d	Cl	31—31.9	53	46.44 (46.16)	3.90 (3.85)		42.78 (42.04)
3e	EtOCO	54.5—57.7	81	53.31 (53.16)	5.22 (5.25)		23.72 (23.55)
3f	NC	86.5—88	45	53.79 (53.64)	4.06 (3.92)	6.27 (5.91)	28.71 (29.92)

neither to σ nor to σ_R, the correlation coefficients did not exceed 0.90. It should be noted that even the chemical shifts of the methylene protons of the hydrodisulfides were not represented by the Hammett equation. These complicated results remind us of the restricted rotation of the sulfur-sulfur bond.[8] If it is true that the sulfur-sulfur group in the phenyl hydrodisulfide was almost fixed in the same plane as the benzene ring, the CH_2–S–S–H group would be relaxed in motion owing to its methylene carbon, and this relaxation would bring about a deviation from a correlation with the chemical shift.

The chemical shifts of acetyl disulfides **3** and **5** were also measured in connection with the above compounds. The shifts of methyl protons of **5** showed no relation for σ or σ_R. A similar relaxation of the restricted rotation of S–S bond can be also seen in this case. The differences among the chemical shifts of the methyl protons of **3a**—**f** are small; these protons seem too distant from the substituents for any substituent effect to be detected. Also, the methylene protons of these compounds were not connected to the character of the substituents.

Experimental

Melting points are corrected. NMR spectra were recorded on a JEOL MH-100 Spectrometer using carbon tetrachloride or deuteriochloroform as solvent and TMS as internal lock. Chemical shifts were determined by use of a frequency counter. The chemical shifts reported in Table 1 were values at infinite dilution, which were obtained by extrapolation of four concentrations (2.5, 5, 7.5, and 10 w/v%).

Benzyl hydrodisulfide[5] and acetyl *p*-substituted phenyl disulfides[1] were obtained by the procedures described previously.

*N-(*p*-Substituted benzylthio)succinimides (**2a**, **2b**, and **2d**)* were prepared by the reaction[3] of *N*-chlorosuccinimides with *p*-substituted α-toluenethiols.[9] Two recrystallizations from ethanol (70 °C) gave **2a**, mp 139.2—140.2 °C (22%); **2b**, mp 180.7—181.3 °C (26%); **2d**, mp 188.2—189.5 °C (35%).

Found for **2a**: C, 57.18; H, 5.21; N, 5.27; S, 12.11%. Calcd for $C_{12}H_{13}O_3NS$; C, 57.35: H, 5.21; N, 5.57; S, 12.76%.

Found for **2b**: C, 61.37; H, 5.56; N, 5.73; S, 13.19%. Calcd for $C_{12}H_{13}O_2NS$: C, 61.25; H, 5.57; N, 5.95; S, 13.62%.

Found for **2d**: C, 51.75; H, 3.89; N, 5.30; S+Cl, 25.57%. Calcd for $C_{11}H_{10}O_2ClNS$: C, 51.67; H, 3.94; N, 5.48; S+Cl, 26.40%.

Acetyl p*-Substituted Benzyl Disulfides.* *A. Procedure for **3a**—**d***: These compounds were obtained by a method similar to that of thiolsulfonate synthesis from *N*-(*p*-tolylthio)succinimide and *p*-toluenesulfinic acid.[4] A mixture of **2a** (7 mmol), thioacetic acid (7.35 mmol, 5% excess), and benzene (30 ml) was stirred for 2 hr at room temperature. The mixture was allowed to stand overnight. The white precipitate of succinimide formed was filtered off. The filtrate was evaporated under reduced pressure. Crude **3a** was crystallized out from the solution of the residue in petroleum ether by cooling (−18 °C, then 2 °C). Immediate pumping out of the solvent after recrystallization from petroleum ether (2 °C) produced 77% yield of **3a** with mp 22 °C. Disulfides **3b** and **3d** were prepared similarly. Disulfide **3c** obtained by Procedure A showed mp 54.5—56 °C (*cf.* by Procedure B, mp 54—55 °C). The analytical data is summarized in Table 2.

*B. Procedure for **3e** and **3f***: To a solution of *p*-ethoxycarbonyl-α-toluenethiol (10 mmol) in ether (20 ml) was added a solution of acetylsulfenyl chloride (10 mmol) in carbon tetrachloride with stirring and cooling (−2 °C to −5 °C) for 10 min. After 1 hr, the solution was evaporated *in vacuo*. To the residue 3 ml of petroleum ether was added, and then the treatment described in A was followed. Disulfide **3e** was obtained in a good yield. Disulfide **3f** was prepared similarly; its analytical data as well as those for **3e** are listed in Table 2.

p*-Substituted Benzyl Hydrodisulfides.* A mixture of acetyl *p*-substituted benzyl disulfide (**3a**, **3b**, **3d**, **3e**, or **3f**, 0.5 g) and 0.83 M ethanolic hydrogen chloride (6 ml) was stirred at 26—28 °C under a nitrogen atmosphere. After several hours (4 hr for **3a**, **3b**, and **3d**, 5 hr for **3e**, and 7 hr for **3f**), the resulting solution was evaporated under reduced pressure. The oil obtained was distilled under vacuum. On distillation, *p*-methoxybenzyl hydrodisulfide **4a** was unstable and its major portion decomposed. *p*-Cyanobenzyl hydrodisulfide **4f** was quite unstable and decomposed immediately after its formation, unless it was dissolved in solvents such as carbon tetrachloride and chloroform.

Such being the case, the NMR spectrum of **4f** was measured using a carbon tetrachloride solution of a neat sample without distillation. It was confirmed with all the other hydrodisulfides mentioned here that the differences between the chemical shifts of a sample obtained from distilled hydrodisulfide and those without distillation were within 0.5 Hz (av. 0.2 Hz).

The yields and boiling points of the hydrodisulfides were as follows: **4a** 2.5%, *ca.* 90 °C, decomp/0.01 mmHg; **4b**, 38%, 91—96 °C/0.02 mmHg; **4d**, 54%, 90—95 °C/0.01 mmHg; **4e**, 18%, 117—120 °C/0.01 mmHg.

References

1) S. Kawamura, T. Horii, and J. Tsurugi, *J. Org. Chem.*, **36**, 3677 (1971).

2) In the previous paper, chemical shifts were shown by frequencies form TMS at 60 MHz. They were re-calculated to τ, for comparison with the present data at 100 MHz.

3) Y. Abe, T. Nakabayashi, and J. Tsurugi, This Bulletin, **46**, 1898 (1973).

4) Y. Abe and J. Tsurugi, *Chem. Lett.*, **1972**, 441

5) J. Tsurugi and T. Nakabayashi, *J. Org. Chem.*, **24**, 807 (1959).

6) S. H. Marcus and S. I. Miller, *J. Phys. Chem.*, **68**, 331 (1964). The correlation, $\tau_{SH} = -0.283\sigma + 6.760$ ($r = 0.993$), has been reported.

7) S. H. Marcus, W. F. Reynolds, and S. I. Miller, *J. Org. Chem.*, **31**, 1872 (1966).

8) W. A. Pryor, "Mechanisms of Sulfur Reactions," McGraw-Hill Book Co., Inc., New York (1962), p. 19.

9) a) E. E. Reid, "Organic Chemistry of Bivalent Sulfur," Vol. I, Chemical Publishing Co., Inc., New York, N. Y. (1958), p. 32. b) "Beilstein," EII, Vol. 10, p. 142.